complete lateral visualization of the third ventricle, of the aqueduct, and the fourth ventricle. In our experience the only certain way to do this is to inject thorotrast, but we are not at all sure that thorotrast is safe in such cases. When thorotrast gets into the sub-arachnoid space it produces shock. If the ventricular system is open, the shock occurs during the radiographic examination, and the patient is in good condition to withstand it. If the ventricular system is closed, the shock occurs when the block is relieved, and this relief is only obtained towards the end of a long operation, when the patient is in the worst possible condition to combat it. So far it is wiser to attempt visualization of the third ventricle with air than with thorotrast.

Ventriculography gives essential information which can be obtained at present in no other way, but it is safer to regard it as part of an extensive surgical operation than as a simple diagnostic procedure. My remarks, of course, have been confined to ventriculography in cases of brain tumour associated with increased intracranial pressure.

Specific Desensitization in Ocular Tuberculosis: An Account of Cases

By J. Allison Corkey, M.D., F.R.C.S.I., D.O.M.S.,
from the Benn Hospital, Belfast

The method of treatment which is carried out by Meller and Urbanek in Vienna in dealing with tubercular affections of the eye is of interest in that it illustrates a new principle in the therapeusis of this disease, namely, that of desensitization of the patient who is considered to have an allergic sensitivity to the protein of the tubercle bacillus.

In introduction, a brief account may be given of the eye conditions which these authorities consider to be due to tuberculosis and of the rationale which underlies this form of treatment.[1]

Allergy as a Factor in Ocular Tuberculosis.

According to Urbanek, the underlying cause of any inflammation in the eye may be tuberculosis. He recognizes a general condition of chronic miliary tuberculosis in which from time to time showers of emboli are distributed from an almost quiescent tuberculous focus by the blood-stream, causing numerous miliary nodules throughout the tissues. The condition is recovered from, and in most areas of the body the tracts of the lesion, being small, are rapidly covered up. In the eye, however, owing to the delicacy of its structure, even this minimal inflammation causes an important lesion, and its progress can be watched through all stages. According to the site of lodgment of the embolus in the sclera, iris, choroid, or retina, there is set up a corresponding inflammation.[2]

The difference in the pathological picture between the primary reaction in an organism infected with the tubercle bacillus and the reaction in secondary sites is

a well recognized phenomenon.[3] In order to account for this fact, one may recall that the tubercle bacillus, in addition to elaborating tuberculo-toxin, contains, or rather is composed of, proteins.

It is possible that the altered reaction to the secondary infection is due to an alteration in the sensitivity of the body-fluids to this protein factor rather than to the toxin. To put the matter in another way, the body has become allergic to the tuberculo-protein, and the type of lesion which is called by pathologists a secondary reaction has a double basis—the response due to the tuberculo-toxin is overlaid by the allergic response caused by sensitivity to tuberculo-protein.

Now, all lesions of the eye as described above are secondary, and on this theory are due in part to an allergic response. Furthermore, it is possible that in a person who has had such a lesion, and whose tissues remain in a sensitive state, the condition may be lit up again by the introduction of the sensitizing agent into the body, or even by the introduction of some other protein (thus giving rise to a non-specific reaction). In this case a lesion may be present without there being any tubercle bacilli at the site of the lesion, but only a localized allergic sensitivity due to a previous tubercular inflammation.

Recognition and Treatment of Hypersensitivity.

If one takes this view of the condition, the therapeutic problem resolves itself into the desensitizing of a patient whose tissues present an allergic response when confronted with a specific protein. Meller and Urbanek use for this purpose a substance known as Toeniessen's "tebeprotin," which the manufacturers claim contains the protein element of the tubercle bacillus without including the toxin.

Before embarking on the treatment of a case believed to be of this nature, every endeavour should be made to exclude other possible causes, e.g., syphilis, gonorrhœa, diabetes, and focal sepsis, and it should be ascertained that there is no gross pulmonary tuberculosis. (Urbanek finds minor gland infection to be the rule.)

If these conditions can be excluded, the patient is admitted to hospital for a skin test, to investigate for hypersensitivity to tebeprotin. This is done after it has been ascertained that the patient while at rest in bed has no pyrexia when the temperature is taken every four hours. Successive tests are made with gradually increasing doses administered, with a control, intradermally on the arm, until either a positive reaction has been obtained or the patient has been shown to have no hypersensitivity to the substance. A positive reaction is one in which the diameter of the reactionary swelling exceeds 3 c.m. after forty-eight hours.

The initial therapeutic dose is one-tenth of that which gives a positive reaction, and gradually increasing injections are given up to a maximum of five-hundredths mgm. The injections are given at regular intervals over a period of several months. A warning must here be given that it is possible to precipitate a catastrophe by an unwise injection of protein, either by giving too large an amount or by letting too long a period elapse between injections and so allowing an anaphylactic state to arise. The disaster may occur in the eye, or other tuberculous lesion, as an excessive focal reaction, or there may be a generalized anaphylactic shock. It is probably on

account of such misadventures that tuberculin therapy has at times fallen under a cloud, but trouble can be avoided if sufficient attention is given to the dosage and the timing of the injections. The difficulty of deciding what initial dose should be given is solved by the skin test, which ensures that the initial dose is not excessive and is on the other hand sufficiently potent to exert some effect.

The following cases seen and treated at the Benn Hospital during the past two years are an illustration of the indications for treatment. In general it may be stated that if benefit is going to ensue, it is noticed at an early date, in some cases even immediately after the diagnostic skin injections.

Cases.

Case I—S. D., male, aged 33. Right retinal detachment. No hole could be found, and the condition was considered to be due to choroiditis on account of a small, fairly recent choroiditic lesion in the portion of the retina that was not detached. The Wassermann reaction was negative, but there was a previous history of treated spirochætal infection. Tebeprotin skin tests were done, and he reacted positively to dilution II. He was given sixteen injections over a period of three months, increasing up to the maximum. The eye condition at the end of treatment was unchanged, but the patient found his general condition much improved.

Case II—L. G., male, aged 28. Keratitis and iritis, right eye. Wrinkling of Decemet's membrane. Numerous synechia of iris to lens capsule. The slit lamp revealed early signs of iritis in the left eye also. The synechiæ in the right eye were completely ruptured by the use of mydricaine, but ten days after the onset there was obvious K.P. in either eye. The Wassermann reaction was negative. The patient was admitted for testing with tebeprotin, and found to be sensitive to dilution II. He was given injections over a period of four months, during which his eye condition progressively cleared up. Seen recently, a year later, the eye was quiet and the only trace of the inflammation was a few small tags of pigment on the lens capsule. Vision in each eye 6/6.

Case III—D. L., female, aged 16. Choroiditis. The right eye was blind from an old injury received in early childhood. For some days the patient had noticed a 'spot' before the left eye situated on the temporal side of the fixation spot. On the morning of the day when she first came to hospital she wakened up to find that the left eye had become blind, and she had to be led into the out-patient department. The vision was reduced to seeing hand movements only, and through considerable vitreous opacity a focus of choroiditis was made out on the nasal side of the disc.

There was K.P. present, and the slit lamp showed very numerous floating cells in the aqueous. She was admitted to hospital for investigation and treatment. Treatment consisted in leeching and atropinizing the eye and administering mist. sod. salicyl. The Wassermann reaction was negative. The patient was found to be sensitive to dilution I of tebeprotin. Regular injections were given over a period of four months, during which time the condition gradually cleared up, leaving a minimal amount of destruction of the choroid. At the end of that time the visual acuity, with correction, was 6/9 partly. When last seen, ten months after

the onset of the trouble, the condition had been maintained, the visual acuity was 6/9, and the small degree of destruction caused by the disease was emphasized by the considerable proliferation of retinal pigment which had taken place at the site of the inflammation. (A more severe inflammation would have destroyed these pigment cells and left a white area with a pigmented margin.)

Case IV—M. L., female, aged 22. Eroding lesion of right upper lid, which had been present three months when patient was first seen. The condition was said to have started as a small pimple, and vaccine treatment had already been given without effect. The middle portion of the lid had been eaten into, and the margin and hair follicles here had been destroyed. The Wassermann reaction was negative, but in spite of treatment for two months more the lesion showed no tendency towards healing. She was admitted to hospital, and showed a positive reaction to dilution I of tebeprotin. The lesion healed rapidly after the diagnostic injections. A possible factor in this result was the use for one day during the test of a vaccine filtrate containing ointment. Tebeprotin injections were given over a period of two months, increasing to the maximum doses. The lesion has remained healed.

Case V—L. M., female, aged 22. Diffuse retino-choroiditis, right eye, giving rise to detachment of retina. Wassermann reaction negative. No hole could be found in the retina. Tebeprotin test : sensitive to dilution II. Injections given over a period of five months. No improvement.

Case VI—F. E., female, aged 35. Chronic choroiditis, left eye. The right eye had been removed some years previously on account of pain. The sight in it had been destroyed by a similar inflammation. The origin of the trouble had been ascribed to an operation for squint in childhood, and the left had been the squinting eye. On examination, central vision was found to be absent and the visual field was limited to the lower temporal region. The fundus presented the picture of disseminated choroiditis, most of the lesions being old. There was, however, a region where the disease appeared active, and the patient complained that her vision was getting worse. The blood sedimentation was found to be much raised. The response to the tebeprotin test was atypical. There was no skin reaction, but the patient was considerably upset generally, and showed a temperature of 100.6 degrees following the use of dilution II. She was started on a dose one-tenth the strength of that which produced the reaction and worked up to the maximum dose over a period of six months. The patient reported that she found her vision much improved.

Case VII—S. M., female, aged 59. Right eye had been removed following inflammatory disease thirty years previously. Left eye had been diseased since childhood. The patient complained of flashes of light coming frequently before the left eye. Examination revealed extensive old-standing choroiditis. The lens had been dislocated, and was seen lying in the vitreous. There was a family history of phthisis, and the patient had recently been much troubled with Bazin's disease. To the tebeprotin test she showed a strong reaction with dilution II. Injections were started, and have now been given for four months. The flashes of light now occur very seldom, and since commencing the injections no further nodules have appeared on the shins.

Case VIII—H. W., male, aged 21. Left choroiditis. The patient, whose vision in the left eye was 6/6, complained of failing vision in this eye. There was seen to be a ring of choroiditic spots around the macula. Wassermann reaction negative. The tebeprotin test was positive to dilution II. The patient lived in the country and did not return for injections.

Case IX—D. R., male, aged 34. Iritis, left eye. The patient was first seen after the eye had been inflamed for one week. There was marked ciliary congestion, and the iris vessels were much dilated. With the slit lamp, cells could be seen floating in the anterior chamber. In spite of treatment, no improvement had taken place two weeks later. The Wassermann reaction was negative. Tebeprotin positive to dilution I. The patient was given injections up to the maximum over a period of three months. The eye settled down rapidly following the initial diagnostic injections. Seen a year later, the eye was perfectly quiet, except for one old posterior synechiæ, and the vision was 6/6.

Tests were also carried out on a number of cases (scleritis, retinitis, choroiditis, iritis (two cases), and disciform keratitis), where the Wassermann reaction was negative. In these, all adults, there was no reaction to tebeprotin. One case of phlyctenular conjunctivitis in a child which had been very resistant also cleared up during the time she was getting the diagnostic injections, although there was no cutaneous response. A youth (heterochromic cyclitis) also gave a negative result.

Comment.

On account of the limited number of cases here presented, no attempt is made to draw any definite conclusions. There are, however, a few suggestive points that arise :—

1. A number of cases of uveal inflammation give a positive result to the cutaneous test and responded to the use of tuberculo-protein as a desensitizing agent. This applies both to acute and chronic cases, though better end-results have been obtained in acute cases before extensive destruction of tissue has taken place.

2. About one-third of the adult patients examined gave a negative response to the cutaneous test for hypersensitivity to the protein.

3. A proportion of the reacting cases failed to show any improvement after desensitization.

4. The method gauging the initial dose is important. It ensures that the dosage is effective, and yet within the patient's tolerance. Unless care is exercised in the dosage and in the interval between doses, it is possible to do the patient more harm than good.

5. It is difficult to prove that the effect is a specific one. No focal reactions have been noted in the present series, but none were expected on account of the control of the dosage. In Case VIII, in which there was a tuberculous family history and in which as well as the eye disease there were other tuberculous manifestations (Bazin's disease), the therapy seemed to produce an equally ameliorative effect on both lesions. The question can only be settled by the study of many more cases, but the results obtained in this small series seem to indicate that such study would be well worth while.

SUMMARY.

1. Some account is given of the view of Meller and Urbanek that many chronic eye diseases are due to an allergic sensitivity of the tissues to the protein of the tubercle bacillus. They advocate treatment by desensitization, as is done in diseases due to hypersensitivity to other proteins (e.g., hay fever, asthma).

2. A record is given of the results of treatment in a small number of cases. While not successful in every case, the results were sufficiently good to warrant further research in the method.

I wish to acknowledge the kindness shown by Prof. Meller and Dozent Urbanek in demonstrating this method of treatment to me at the First University Eye Clinic, Vienna, and I should like to thank the senior members of the staff of the Benn Hospital for their co-operation in carrying out this work, and in particular Dr. R. S. Allison for his assistance in the general physical examination of the patients.

REFERENCES.

1. URBANEK, *Trans. of the Ophth. Soc. of U.K.*, Vol. 52, 1932, p. 227.
2. TOOKE, *Brit. Jour. of Ophth.*, January, 1936, p. 23.
3. BOYD, "Pathology of Internal Diseases," 1931 Edition, pp. 201, 213.

The Effect of Arsenic Preparations (Neoarsphenamine and Silver Arsphenamine) on the Protein Fractions of Blood Plasma in Syphilis and Disseminated Sclerosis

By D. C. PORTER, M.B., B.CH.,

from the Department of Pharmacology, Queen's University, Belfast

IN the course of a study of the alterations in some physico-chemical properties of the blood following various therapeutic and diagnostic measures, the blood-plasma protein fractions were examined in a series of cases, before and after injections of arsenic. Ten patients were examined. Nine of these suffering from primary syphilis were treated with neoarsphenamine, and one suffering from disseminated sclerosis was treated with silver arsphenamine. The subjects used were chosen at random from the venereal out-patient department of the Royal Victoria Hospital, Belfast.

The method used for separation of the plasma protein fractions is that described by Peters and Van Slyke (1932), a modification of the method originally used by Howe (1921). In this method sodium sulphate solutions in strengths of twenty-two per cent. and fourteen per cent. are used for the precipitation of total globulin and euglobulin plus fibrinogen fractions respectively. These solutions are super-saturated and necessitate precipitation in an incubator at 37°C. The fibrinogen fraction was estimated by recalcifying the plasma and washing the clot with saline. The total plasma protein was estimated directly using a 1 in 25 solution in 0.8 per cent. sodium chloride. The nitrogen estimations were done by the micro-Kjeldahl